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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/500,904	02/09/2000	John B Harley	OMRF 161 CIP	3202

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EXAMINER
FOLEY, SHANON A

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/10/2002

39

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/500,904	HARLEY ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 14 August 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ they raise the issue of new matter (see Note below);
   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____.
3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see the correspondence attached*.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: —.
   Claim(s) objected to: —.
   Claim(s) rejected: *6-10 and 19-22*.
   Claim(s) withdrawn from consideration: _____.
8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). 892
10. ☒ Other: *See Continuation Sheet* 892

DETAILED ACTION

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 6-10 and 19-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 35 of copending Application No. 08/781,296 for reasons of record. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

In response, Applicant states that a terminal disclaimer will be filed upon indication of allowable subject matter.

This rejection is maintained for reasons of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-10 and 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Applicant summarizes claim 6 (indicated as claim 1 on page 2 of the response) and asserts that the skilled artisan would be able to interpret the meaning of the claim because the instant diagnostic assay is similar to immunoassays routinely used in the art.

Applicant's arguments have been fully considered, but fail to clarify the meaning of the claims. It is maintained that the "means for determining" step does not correlate with the objective to "predict the risk of developing lupus" in the preamble of the claim. As discussed previously, risk factors for distinguishing whether a subject will develop lupus or whether a subject has a chance of developing lupus has not been established by the claimed assay.

It appears that Applicant has acquiesced to the rejections of claims 7 and 20 because Applicant has offered no response to the rejections of these claims. These rejections are maintained for reasons of record.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-10 and 19-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

Applicant states that there is a genetic component with lupus and "there are tests that can be performed to indicate if an individual is more likely than the average individual to develop a disorder, in this case, lupus". Applicant states that it is well established that individuals with elevated titers of EBV have a greater risk of developing Burkitt's lymphoma and nasopharyngeal

carcinoma, as taught in the instant specification. Applicant states that cause and effect between lupus and EBV does not have to be established, but whether the test yields a more probable outcome than not. Applicant has included abstracts to provide evidence that EBV is associated with lupus.

Applicant's arguments have been considered, but are found to be unpersuasive. Applicant has not indicated any evidence that would indicate that tests exist for determining the likelihood of developing lupus. The art does not indicate exposure to EBV correlates with developing lupus and the specification does not provide an enabling disclosure for an assay to predict the likelihood of developing lupus. Applicant states above that the risks associated with developing Burkitt's lymphoma and nasopharyngeal carcinoma are also attributed to elevated titers of EBV. Therefore, the skilled artisan would not be able to conclude from the assay whether an individual with elevated titers of EBV is at risk for developing any number of unrelated diseases, much less one in particular. There has been no evidence that suggests that the test would lead to any determinable outcome or provide any probable conclusion that an individual is more likely to develop lupus, Burkitt's lymphoma or nasopharyngeal carcinoma.

The abstracts applicant has provided do not overcome the instant rejection. The abstracts offer no conclusive data that would indicate that exposure to EBV leads to a greater risk of developing lupus than any other disease. The abstracts only speculate the relationship between EBV infection and the development of lupus. Verdolini et al. only discusses one subject that developed lupus after exposure to EBV and postulates the association between virus and autoimmune disease. This one subject would not indicate that the skilled artisan would recognize EBV as a major risk factor for developing lupus in the general population. Dror et al.

states in the first sentence that lupus "...is a multisystem disease of unknown origin...", which supports the conclusions in the previous Office action. The reference also discusses only one subject to illustrate the possible relationship between EBV and lupus. James et al. selected 196 lupus patients and screened them for previous exposure to various viruses. Although almost all of the patients had had prior exposure to EBV compared with the other viruses, it is also noted that the vast majority of "controls", i.e. 95%, also had been previously exposed to EBV. James et al. does not provide data that would indicate factors that a subject would be more likely for developing lupus or any other disease upon EBV exposure. There is no data in the prior art or the specification that would indicate that exposure to EBV is a risk factor for developing lupus or that detecting an antibody to EBV would indicate a predisposition for developing lupus. Marchini et al. (Journal of Autoimmunity. 1994; 7: 179-191) teaches detection of lupus requires the detection of anti-EBNA antibodies as well as autoantibodies specific for SmD, see the abstract and the discussion section. The teachings of Marchini et al. clearly demonstrate that the instant claims are deficient for detecting the risk of developing lupus since more than one factor is required to assay for lupus.

As discussed in the previous action, one skilled in the art would doubt that identification of a single antibody in an assay would predict the risk for developing lupus because there are other unidentified factors that may lead to autoimmune disease. Carson teaches that there are many obstacles for predicting autoimmune disease since several genes can increase susceptibility of autoimmune disease or influence immune responses to infectious agents that may trigger autoimmunity. Furthermore, even genetically identical individuals have different immune systems due to the somatic generation of immune diversity, which further indicates improbability

of predicting the outcome of a changing environment. The specification does not address these concerns in the art and the instant assay and method do not take these factors into account.

Therefore, due to the lack of direction or examples conclusively correlating evidence that EBV causes autoimmune disease, the state of the art and the lack of predictability by one skilled in the art to determine the probability of development of autoimmune disease, it is maintained that there an undue amount of experimentation would be required of one skilled in the art to practice the invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley
September 6, 2002

JAMES HOUSEL 9/9/02
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Continuation of 10. Other: PTO-892 and reference: Marchini et al. Journal of Autoimmunity. 1994; 7: 179-191..